

A spotlight on Dr. Linyee Shum

By Diana Nieves
LRG Program Associate

In our last issue, we broke the news that after a brief hiatus, plasma testing would begin again on May 16, 2011. This action is due to months-long exhaustive efforts by the Life Raft Group and Dr. Linyee Shum of TDM Pharmaceutical Research to resume this process as quickly as possible without putting financial burden on the patient. We wanted to show the GIST community Dr. Shum's persevering and generous nature by profiling him in our newsletter.

Dr. Linyee Shum's career path began the moment he was born. It appeared he was destined to be an engineer and was encouraged to pursue it since early childhood. He even majored in mechanical engineering during his freshman year of college. However, he took an unexpected turn on his journey. Dr. Shum earned bachelor degrees in Pharmacy and Pharmaceutics and a Ph.D. in Pharmaceutics, specializing in Pharmacokinetics and Drug Metabolism from the State University of New York at Buffalo. He pursued his Ph.D. not so much for the title of being a doctor but

See **SHUM**, Page 8

Battling gastrointestinal stromal tumor



LIFE RAFT GROUP

June 2011

In memory of Ben Redman, Jen Sikes, Nancy Wisecarver Jones, Dana O'Bryan, Mariette Dubois, Steven Bashaw & Wendy Warren

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Mutational testing & survival: where we stand

By Jerry Call
LRG Science Coordinator

Only six percent of GIST patients in the United States take advantage of testing that could be used to individualize their treatment according to a new article in the *Annals of Oncology*. Dr. Peter Pisters of MD Anderson Cancer Center in Houston, Texas and his colleagues reported results of the GIST reGISTry, a Novartis Pharmaceuticals-supported registry of 882 GIST patients in the United States.

According to the study authors, "This study pointed out several differences between clinical practice and clinical practice guidelines such as those by Na-



CALL

tional Comprehensive Cancer Network (NCCN)¹ and the European Society of Medical Oncology (ESMO)². Although the majority of patients had GIST as the original diagnosis, there was poor utilization (6%) of KIT mutation testing of tumors despite KIT mutation testing being a standard practice at several academic centers, as well as recommended by both NCCN and ESMO. The authors speculated that the lack of mutational testing "...May be due to limited access to centers where testing is carried out, a lack of knowledge of the benefits of the

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Alianza GIST meets for second time in Brazil

By Sara Rothschild
LRG Global Relations Director

At the end of 2009, The Life Raft Group proudly announced the foundation of an important initiative, the Latin American GIST Coalition, now called Alianza GIST. Currently comprised of twelve countries, this group of patient advocates from across Latin America has formed a partnership dedicated to



Rafael Vega, Norman Scherzer, Rafael Becerra, and Sara Rothschild

improving the survival and lives of GIST patients in Latin America.

In February 2010, the country representatives first met in Monterrey, Mexico, accompanied by reps from the LRG and The Max Foundation. Rodrigo Salas, the Mexican representative of the Coalition, summed up the purpose of the meeting as "an extraordinary historic event paired with expertise from our partnership organizations to strengthen our efforts at promoting survival of GIST

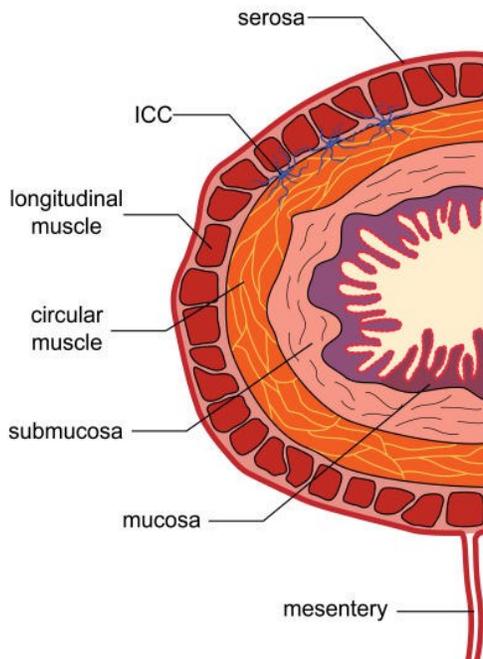
See **BRAZIL**, Page 9

The connection between ICCs & GIST

By Alon Hawkins
LRG Associate

Where does GIST come from? Good question. GIST actually begins formation in special cells called interstitial cells of Cajal (ICCs). ICCs are considered the pacemakers of the GI tract because they send signals to the muscles instructing them to move food and liquid through the digestive system. These cells are specially located in the muscular layers of the wall aligning the gastrointestinal tract, which can be present in any digestive organ except the esophagus.

The presence of the KIT protein distinguishes GISTs from other similar tumors. KIT receptors and GIST cells show the same type of differentiation, so tumor cells test positive for GIST approximately 85 percent of the

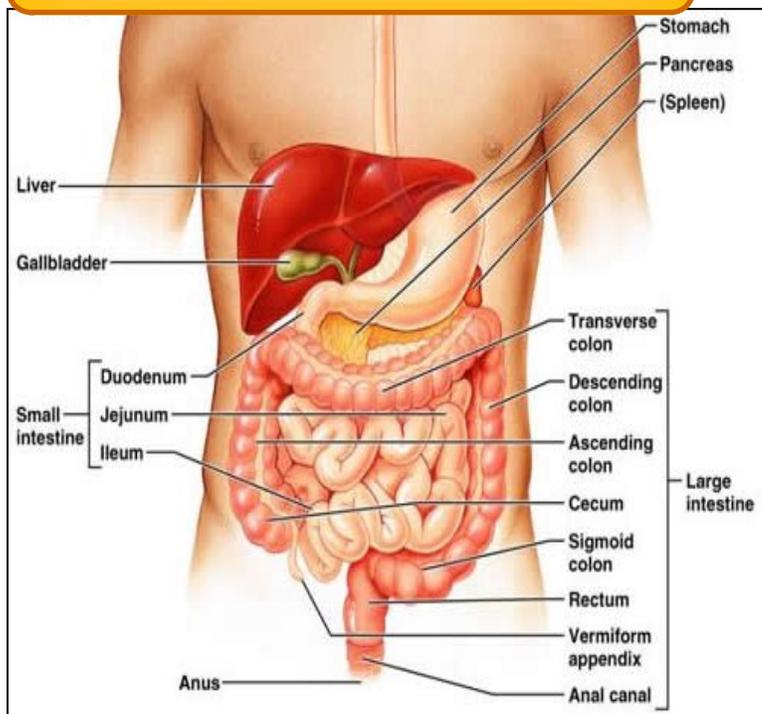


time. As a result, most GIST cases are believed to be caused by a mutated KIT gene and the resulting malformed KIT

protein triggers abnormal cell division and tumor growth.

In normal ICCs, KIT triggers cell division only when a cell needs to be replaced. In abnormal ICCs, a mutation occurs in the KIT gene causing the KIT receptors to signal uncontrolled growth. This uncontrolled growth causes a GIST to form. Other abnormalities may occur during tumor development in the GIST

ICCs are considered the pacemakers of the GI tract



The Life Raft Group

Who are we, what do we do?

The Life Raft Group (LRG) directs research to find a cure for a rare cancer and help those affected through support and advocacy until we do. The LRG provides support, information and assistance to patients and families with a rare cancer called Gastrointestinal Stromal Tumor (GIST). The LRG achieves this by providing an online community for patients and caregivers, supporting local in-person meetings, patient education through monthly newsletters and webcasts, one-on-one patient consultations, and most importantly, managing a major research project to find the cure for GIST.

How to help

Donations to The Life Raft Group, a 501(c)(3) nonprofit organization, are tax deductible in the United States. You can donate by **credit card** at www.liferaftgroup.org/donate.htm or by sending a **check** to:
The Life Raft Group
155 US Highway 46, Suite 202
Wayne, NJ 07470

Disclaimer

We are patients and caregivers, not doctors. Information shared is not a substitute for discussion with your doctor.

Please advise Erin Kristoff, the Newsletter Editor, at ekristoff@liferaftgroup.org of any errors.

cells, but abnormal KIT activation is the primary cause. In wild-type GISTs cases, growth triggers have yet to be identified, though research continues.

The first steps towards finding a cure for GIST can start with you!

If you or your loved one has had their tumor removed, you are eligible to participate in the GIST Collaborative Tissue Bank (GCTB).

As an added benefit, we also offer free mutational testing with participation.

Contact the LRG at 973-837-9092 to learn about GCTB, and how you can help find a cure for GIST.

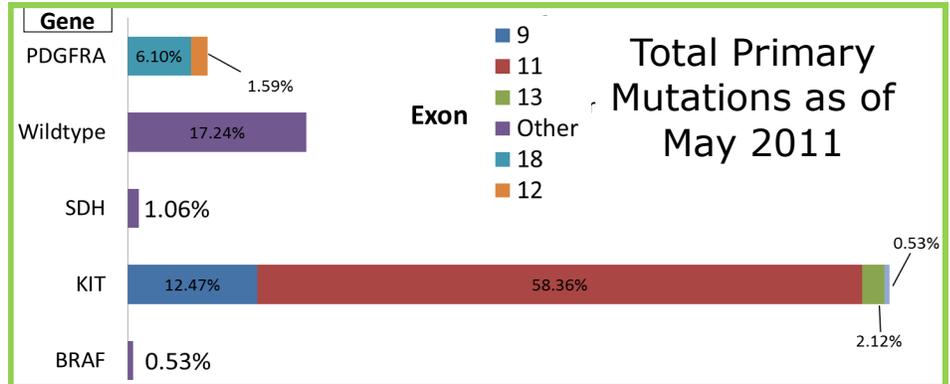
State of the GIST Community Part 3: What do we know about mutational testing?

By Magda Sarnas

LRG Patient Registry Supervisor

The Life Raft Group has vocally supported mutational testing for many years. Countless articles have been written in prior LRG newsletters about what this testing is, how it can be beneficial to treatment, and even about trials that target a specific mutation. However, as of May 1, 2011, the LRG patient registry only received 377 reports of mutations out of 1,327 patients, which only represents **28 percent** of the entire registry. Part of this may be related to the fact that mutational testing is not common practice at diagnosis, or some patients, guided by an oncologist's care, might feel it is unnecessary to perform the test if they have been stable or disease-free for more than a few years. Regardless of the whys, we are still able to identify certain trends, even with a small population.

What we do know from the LRG's data is that a primary mutation in the KIT gene accounts for 73 percent of this group. Of the total group 58.36 percent of these reports are patients with the KIT Exon 11 mutation. Exon 9 represents



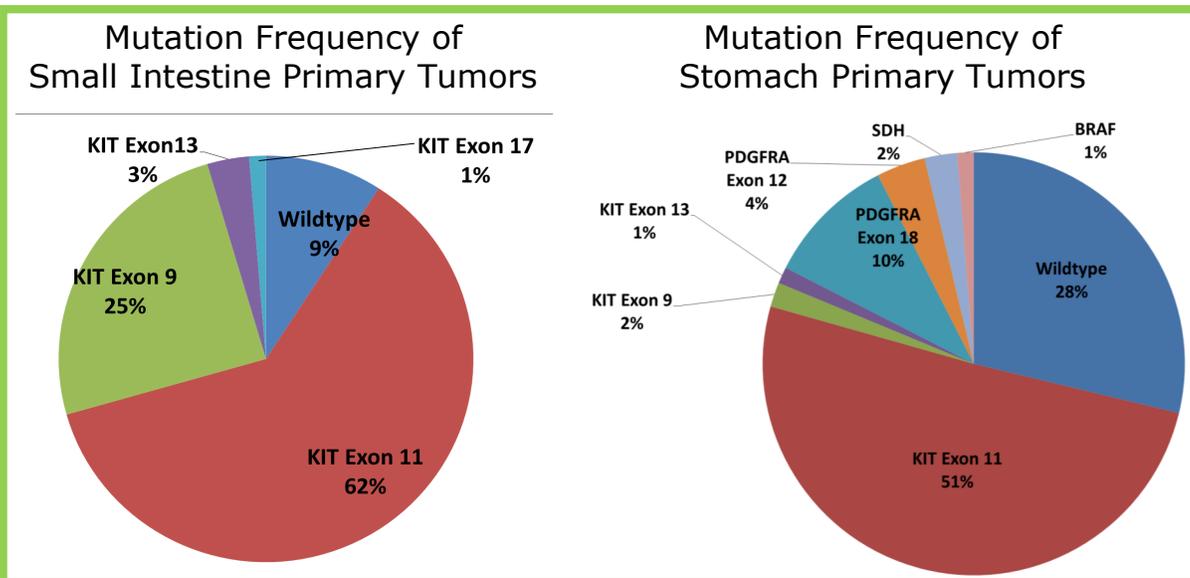
12.47 percent of the total group and exon 13 makes up only 2.1 percent. While wildtype patients make up 17 percent of the group, we are seeing a few patients identifying their mutations as BRAF or SDH mutations. Lastly, patients with the PDGFRA mutation are comprised mostly of Exon 18, which is 6.1 percent, and the majority of Exon 18 does have the D842V mutation. We have less than two percent who have the exon 12 mutation.

Mutations in the Stomach and Small Intestine

A common question that is asked is if a particular mutation is commonly associated with a primary tumor location. What we have seen with primary tumors located in the small intestines and the

stomach is that in both locations, Exon 11 mutations appear in more than 50 percent of diagnosis. While we have received more reports of exon 9 in 25 percent of cases with a primary in the small intestines, this mutation has only appeared in two percent of cases in the stomach. The reverse is seen in wildtype mutations, where 28 percent are seen in the stomach, while only nine percent are diagnosed in the small intestines. With other rare mutations such as PDGFRA and SDH, we have not received any reports of these mutations appearing in the small intestines, but more so with primary tumors located in the stomach. However, with tumors that appear at junction points we have obtained one report of PDGFRA exon 18 appearing in the

stomach and small intestine junction area. With tumors that appear at the junction of the esophagus and stomach, we have seen at least four cases with the mutation exon 11 and one with exon 9. Exon 13 mutations occurred in the small and large bowel and the rectum and not in the stomach.





Healthcare 2011 and beyond: Part 3



By Diana Nieves
LRG Program Associate

In our last newsletter, we covered some resources available to you to cover your prescription drugs outside of Medicare, in this last article in the series, we will look at pharmaceutical company assistance.

Help from Pharmaceutical Companies

If you have exhausted other resources and/or are still in need of assistance to pay for your prescription drugs, help is available through different pharmaceutical companies. The **Partnership for Prescription Assistance (PPA)** - has a directory of pharmaceutical company members that offer patient assistance programs. Visit www.pparx.org/sites/default/files/PPA_Directory.pdf to view that directory.

Below are pharmaceutical companies with prescription drugs utilized by GIST patients:

Novartis is committed to providing access to their medica-



tions for those most in need through the Novartis Patient Assistance Foundation, Inc. (PAF). PAF provides assistance to patients experiencing financial hardship who cannot afford their medicines or the co-pay of their third party insurance coverage to pay for medicines. To be eligible for Novartis PAF, patients must: be a U.S. resident, provide proof of income within program guidelines and not have private or public prescription coverage. Patients must reapply/requalify annually, which you can do at www.pap.novartis.com; 1-866-884-5906. If you have insurance and need

assistance with your co-Pay contact: 1-800-282-7630 <http://www.gleevec.com/patient/patient-resources.jsp>

Pfizer Helpful Answers is a family of assistance programs for people who have no insurance, or who do not have enough insurance and need help getting their Pfizer medicines. Programs may provide: Pfizer medicines for free or at a savings to patients who qualify and/or reimbursement support services to insured patients. GIST patients utilizing Sutent or other Pfizer prescription drugs can apply for:



First Resource Program: Free Pfizer oncology medicines for eligible uninsured and underinsured patients and reimbursement support services for insured patients.

Pfizer Pfriends Program: Savings on Pfizer medicines through your pharmacy, regardless of income. You must have no prescription coverage to qualify.

To learn more about these and other programs provided by Pfizer, call 1-866-706-2400 or visit

www.pfizerhelpfulanswers.com/pages/Misc/Default.aspx. For Sutent access to treatment outside of the United States, visit

www.accesstotreatment.org. This platform was designed and is administered by Axios International, specialists of chronic care systems in developing countries. The goal is for institutions and their patients in developing countries to gain access to medical products.

Bayer - The REACH Program for Nexavar provides reimbursement information and support to assist patients receiving Nexavar. By calling 1.87.REACH.4IT (1.877.322.4448) and a REACH Program counselor can: Answer your



clinical questions about Nexavar and insurance coverage, and also assist you in applying for alternate sources of coverage for Nexavar treatment including assistance for those without adequate coverage.

Help From Other Non-Profit Groups

The following non-profit organizations offer assistance to people who cannot afford medicine or healthcare costs, and in some cases beyond what is received through Medicare/Medicaid. You can also do a search online for other non-profit organizations not listed here by using key words "help with medicine costs" or a similar phrase. Please contact the organization directly to learn more about their services and how they can assist you.

NeedyMeds (www.needy meds.org) is a 501(c)(3) non-profit with the mission of helping people who cannot afford medicine or healthcare costs. The information at NeedyMeds is available anonymously and free of charge. NeedyMeds offers assistance in the following areas: National, Medicare Prescription Drug Assistance, Insurance Copayment Assistance, and Prescription Assistance. Call (978) 865-4115 for assistance.

Partnership for Prescription Assistance (PPA) (www.pparx.org) is a nationwide effort sponsored by America's pharmaceutical research and biotechnology companies. PPA helps uninsured and financially struggling patients without prescription drug coverage get the medicines they need for free or nearly free. They offer a single point of access to more than 475 public and private programs, including more than 180 offered by pharmaceutical companies. PPA member programs offer more than 2,500

Swiss are back at it with 8th annual meeting

By **Helga Meier Schnorf**
GIST Swiss Group

Approximately 90 GIST patients, relatives, GIST experts, interested professionals, physicians and representatives of the pharmaceutical industry gathered in Zurich on April 8, 2011 for the eighth meeting of the Swiss GIST group in the Restaurant *Au Premier* at Zurich Main Station (HB Zürich). A welcome was extended to special guests Anna Costato from Italy, Bertrand de la Comble from France, Candy Heberlein, President of the Swiss Foundation for the Promotion of Bone Marrow Transplantation and Christel Jäger-Freysoldt, Chief Executive of Das Lebenshaus in Germany. Representatives from Bayer, Bristol-Myers Squibb, Novartis and Pfizer were also present. As always, it was a unique opportunity for the participants to learn about the latest insight into Gastrointestinal Stromal Tumors and their treatment, as well as to meet experts. Markus Wartenberg from Das Lebenshaus excelled once again as the presenter. Everyone came to the meeting with their own expectations, and as always, neither participants nor organizers were disappointed. The panel of speakers gave very impressive presentations. As in prior years, simultaneous German/French or vice versa translation was provided.

Completed for the meeting and can be purchased. The aim of this film is to introduce GIST and the exemplary treatment successes to the public at large. The documentary film shows the route from correct diagnosis to treatment and dealing with this cancer, with the aid of case histories. It examines the worldwide networking of patients and physicians, and the collaboration between different medical disciplines and research. The



From left to right: Martin Wettstein, Dr. Michael Montemurro, Helga Meier Schnorf, Markus Wartenberg, Dr. Urs Metzger.

was “Imaging of GIST tumors; what we can display today and what we can expect in the future”.

A very special approach to metastasis surgery was taken by Dr. Markus Weber from Triemli Hospital in Zurich. In his impressive presentation on “The current importance of metastasis surgery”, he explained metastasis surgery notably in the liver with impressive images.

Vito Mediavilla, web master and GIST patient covered the topic, “Social Media”, which aroused a great deal of interest. Vito explained what we mean by Facebook, Twitter and a listserv. Finally, Dr. Philippe Fontaine, a general practitioner and GIST patient, gave a very personal presentation entitled “GIST: My friend!”, in which he described how he handles this disease (See page 10 for a portion of his presentation).

Documentary: “Living with GIST”, Gastrointestinal Stromal Tumour, the model for purposeful treatment

The short documentary film “Living with GIST”, Gastrointestinal Stromal Tumour, the model for purposeful treatment,” opened the Eighth Swiss GIST meeting. The DVD version was com-

pleted for the meeting and can be purchased. The aim of this film is to introduce GIST and the exemplary treatment successes to the public at large. The documentary film shows the route from correct diagnosis to treatment and dealing with this cancer, with the aid of case histories. It examines the worldwide networking of patients and physicians, and the collaboration between different medical disciplines and research. The

2011 Topics

The topic of GIST was handled in two parts with cutting-edge presentations from the two international GIST specialists, Dr. Michael Montemurro and Dr. Peter Reichardt.

Dr. Michael Montemurro (consultant at the Centre Hospitalier Universitaire Vaudois (CHUV) in Lausanne and medical advisor to the Swiss GIST group) spoke about “Treatment for inoperable GIST: drugs, pharmacokinetics, compliance and open-label studies in Switzerland”. Dr. Peter Reichardt, Director of the Sarcoma Center in Berlin-Brandenburg, then presented a paper on “Adjuvant and experimental therapies”.

The third thrilling presentation was given by Dr. Dominik Weishaupt from Triemli Hospital in Zurich. His topic

tion).

The attentive audience demonstrated their appreciation for all of the presentations with resounding applause. This in turn also reflected the high quality of this annual national event.

Following presentations, the second general meeting of patients in the Swiss GIST group began under the support and guidance of Martin Wettstein, President of the Swiss GIST group. This association, which supports all those affected by GIST, was officially formed in January 2010 in Zug. Martin Wettstein presided over this second meeting with his usual aplomb and our sincere thanks go to him too for his work!

President Wettstein provided a worthy conclusion to the general meeting by appointing Dr. Michael Montemurro and Markus Wartenberg, as honorary members of the association. With a few well-chosen words and to resounding applause, Martin Wettstein presented both of them with a certificate of honorary membership.

MUTATIONS

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testing, or possible differences in approach to patients with GIST treated with imatinib.” In the USA reGISTry, only one percent of patients being treated at community-based practices had mutational testing compared to 12 percent of patients at academic centers (6% combined).

The Life Raft Group also maintains a registry of over 1,300 LRG members that are GIST patients from around the world, although the majority are from the United States. This month we will be sharing some of the **data concerning mutational testing from the LRG GIST Patient Registry.**

As of May 17, 2011, the LRG registry had 1,327 GIST patients; 377 (28%) of them have reported mutational testing results to the LRG. This percentage is considerably above that reported in the USA reGISTry and probably indicates a patient membership that is more actively involved in their treatment plan. It is also likely that many LRG members may actively consult and/or be treated at GIST referral centers and these centers are more likely to order mutational testing.

An interesting preliminary observation from the LRG registry noted that overall survival times for patients that had mutational testing is longer than the survival time for those that have not had testing (See Figure 1, October 2010). These survival times are calculated from the

Figure 2: Mutational Testing by Age at Diagnosis

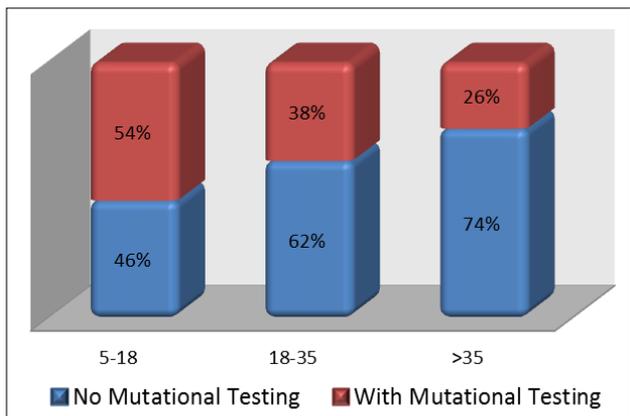
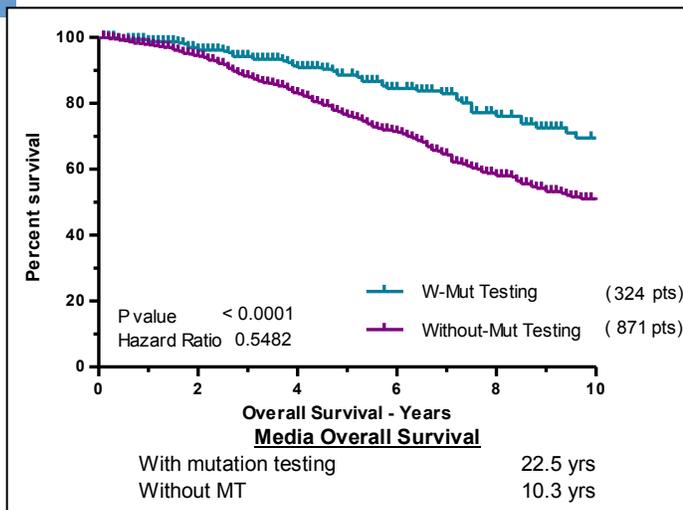


Figure 1: All LRG Patients With or Without Mutational Testing



date of diagnosis.

While this observation is interesting, it doesn't have much context. There are many reasons that aren't related to mutational testing that these patients might have longer survival times. For example, patients with less advanced disease, that are considering adjuvant treatment with Gleevec, might get tested more often than patients with advanced disease. Examples like this, which cause the results to be hard to interpret, are called confounding factors, and there are some known and unknown confounding factors that might affect these survival results. We have examined some of the potential confounding factors that we are aware of and present some of the results in this edition of the newsletter.

Unpublished LRG registry data has verified that, in general, younger patients (under age 35 at the time of diagnosis) have better overall survival than older patients. This is likely to be due to a relatively high percentage of patients with pediatric-type GIST in this age group. Patients with pediatric-type GIST tend to have longer overall survival than patients with adult GIST. In the LRG registry, younger patients reported having mutational

testing more frequently than older patients (see Figure 2). To examine this potential confounding factor, we ran an analysis looking at only patients over age 35 at the time of diagnosis. To further enrich the population, we limited the results to only those with metastatic GIST. The results (Figure 3, Page 7) were very similar to results including all patients (hazard ratio 0.55 for all patients vs. 0.53 for those diagnosed over age 35).

The LRG registry contains data on patients with both metastatic GIST and those with no metastases (“mets”). One possibility is that patients that are having mutational testing have less advanced disease. For example, a doctor considering offering his/her patient adjuvant Gleevec might decide to do a mutational test to verify that the patient was likely to respond to Gleevec. This patient would be likely to have a longer survival time than a patient that already had metastatic disease and the increased survival time would have nothing to do with having a mutational test. This confounding factor represents one of the most likely explanations for the differences observed and we explored this possibility from several different directions.

First we classified patients according to their disease stage. One category was patients that had reported metastases at any time. The second category was patients that had not reported metastases and that regularly and recently reported their status. A third category was patients that had not reported metastases but had not provided a recent update. The last category (15 patients) had seldom, if ever, provided an update beyond initial registration. At first glance this grouping appears to suggest significant differences, but when the two “no mets” groups with and without a recent update are combined and compared to the

MUTATIONS

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“mets” group, the difference in patients with mutational testing is small, 26 percent for no mets vs. 28 percent for mets. So the results of this analysis were not conclusive, or at best, hard to interpret. Patients with mutational testing had a median date of diagnosis of March 22, 2005 compared to a median date of diagnosis of September 9, 2003 for patients without mutational testing.

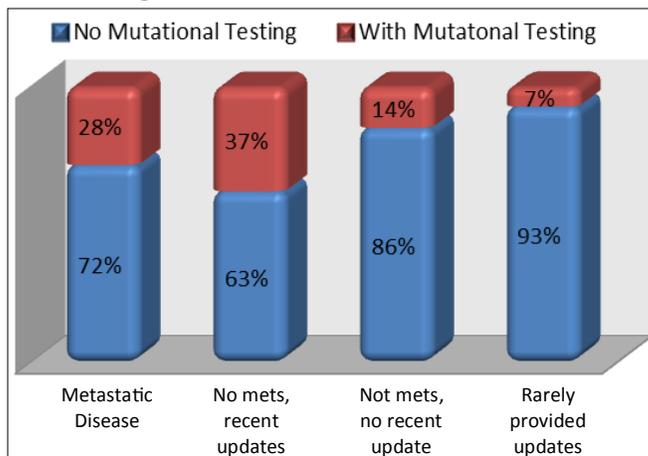
Another way to look at the effect of disease stage was to only look at patients that already had metastatic disease when they were diagnosed. Looking at this group has several advantages. All of these patients are at a similar stage and since they all had metastatic GIST at diagnosis, the confounding factor of adjuvant treatment is eliminated. We compared the survival of 283 members (October 2010) that fit this category. Members without mutational testing had a median overall survival time of 6.3 years. The overall survival time of members with mutational testing was better but could not be defined (p value=0.0071, HR 1.83).

Drilling down a bit deeper into this group, we further divided the group into those diagnosed below age 35 and over 35. When doing this, both groups continued to show a benefit for mutational testing, but the differences were no longer statistical significance, possibly due to smaller sample sizes. When examining the younger group in more detail (Figure 5A, page 11), we find an example of a how a confounding factor might influence results. If we just look at mutational testing, there seems to be a fairly large difference (HR 3.25, median survival of 5.4 years vs. undefined), bordering on statistical significance (P=0.0635). But when we look at the makeup of these groups we find that the group with mutational testing has a higher percentage of females (n=17) compared to males (n=3). In the no mu-

tation testing group, females still outnumber males, but by a smaller margin (14 females; 6 males). Females make up the vast majority of patients with pediatric-type GIST (~85%) and pediatric-type GIST is diagnosed up to age 35 and beyond (unpublished LRG data and others).

This is further demonstrated when looking at the actual mutations in this group, 15 wildtype GISTs and three SDH mutations, both typical of pediatric-type GIST versus only two with KIT mutations typical of adult GIST. Thus in this group, the reason for the longer survival in those with mutation testing may not be related to how the test was interpreted, it may be because this group had more of the “good prognosis” pediatric-

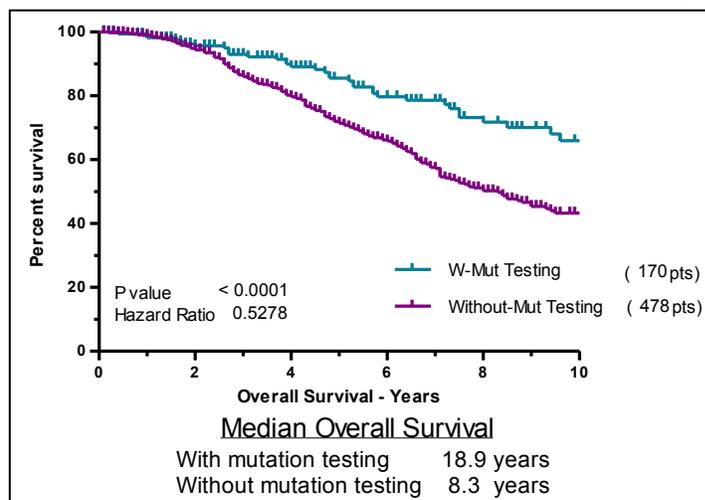
Figure 4: Disease Status



type GIST patients.

The mets at diagnosis, over age 35 group (Figure 5B, page 11) was a bit different however. The group with mutational testing (n=58) appeared to do somewhat better than those without testing (n=185), although the results did not quite reach statistical significance. The median survival of those with mutational testing was 9.4 years versus 6.2 years for those without mutational testing (HR

Figure 3: Metastatic LRG Patients >35 at Diagnosis With or W/O Mutational Testing



1.53, P=0.099). As yet, we have not found a confounding factor to explain the difference (and many would say that because the difference was not statistically significant, there is no difference) and we could speculate that there might be a treatment related difference. Perhaps the doctors of these patients are making mutation dependent treatment decisions. Another possibility is that these patients are very proactive (hence the mutation test) and they consult with or are treated at GIST referral centers where their treatment might be more individualized than in a community setting. Although much work remains to be done in analyzing these results, we know that there are a number of concrete reasons for doing mutational testing today. Mutational testing can be used not only to optimize current treatment, but just as importantly, it can be used to help decide which patients do not need drug treatment, as well as match patients for appropriate trials and clinics in some cases.

How can mutational testing be used?

Dose selection

The right dose in the right patient

Clinical trial results have indicated that GIST patients with KIT exon 9 tumors (about 10-13% of all GISTs) have a

HEALTHCARE

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brand-name medicines, including a wide range of generics. PPA helps patients contact government programs such as Medicaid and Medicare. More than 40 of the assistance programs focus on the medication and health care needs of children. PPA provides information on nearly 10,000 free health care clinics and has connected more than a quarter of a million patients with clinics and health care providers in their communities. PPA also assists patients with chronic disease in learning about the types of new medicines in development that may help them. Call 1-888-4PPA-NOW (1-888-477-2669) for assistance.

The Patient Access Network Foundation (PAN) (www.patientaccessnetwork.org) pro-

vides financial support for out-of-pocket costs associated with a wide range of drugs, to treat a number of conditions. Call 1-866-316-PANF (7263) for assistance.

Patient Services, Inc. (PSI) (<https://www.patientservicesinc.org>) is a 501 (c)(3) non-profit, charitable organization. They provide assistance to patients with chronic illnesses who struggle to keep up with expensive premiums and co-payments. PSI:

- Locates health insurance in all 50 states
- Subsidizes the cost of health insurance premiums
- Provides pharmacy and treatment co-payment assistance
- Assists with Medicare Part D Co-

insurance

- Helps with advocacy for Social Security Disability
- PSI evaluates an individual's financial, medical, and insurance situation to determine who is eligible for premium or co-payment assistance. They provide help for many illnesses and offer many types of financial assistance. If you would like more information about the financial help available from Patient Services for the treatment of any of the diseases listed on their website (GIST is one of these illnesses), please call 1-800-366-7741. PSI's Patient Services Representatives (PSR) can walk you through the online application process as well as mail you appropriate forms and informative literature.

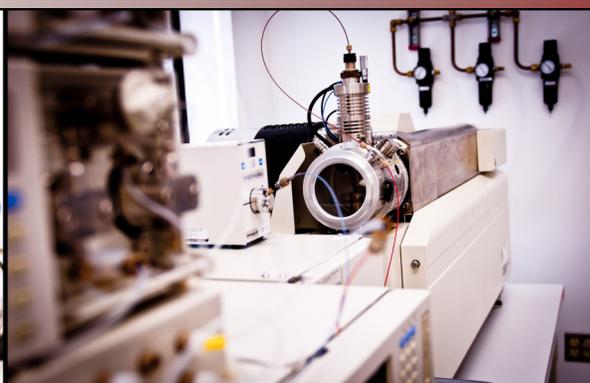
SHUM

From Page 1

as a logical step to further develop his critical thinking skills.

And it is these critical thinking skills that have enabled Dr. Shum to tackle the frontier of science to improve the quality of life for all mankind. For over 25 years, he has been paving the way of pharmaceutical research and development. His focus has been in ADME (absorption, distribution, metabolism and elimination), pharmacokinetic, pharmacodynamics and protein binding. Dr. Shum has been involved in plasma level testing since his early years as an undergraduate when pharmacokinetics was still in its infancy. At the hospitals in Buffalo, he and his colleagues set up a therapeutic drug monitoring service to observe patients that had a narrow therapeutic index (low safety margin).

Dr. Shum feels that plasma level testing will pave the way for medicine in the 21st century. As he detailed, "The one size fits all mentality does not work in today's drug treatments because we



Dr. Shum may be a little camera shy in front of the lens, but that's certainly not true behind the lens. Here are pictures he took of the Liquid chromatography–mass spectrometry machine (LS-MS) used in plasma level testing.

know better, and we have the means to tell us otherwise. We as humans have a diverse genetic makeup. We are all different as well as individually unique. Our bodies process drugs differently and react to drugs differently. Moreover, today's medicines are more potent than ever. A proper therapeutic concentration must be maintained to ensure an effective treatment and minimize adverse side

effects. This will ultimately improve the quality of lives of patients. This has to be the passion of every health care provider."

Dr. Shum's passions are not exclusive to the laboratory. He is a very outdoorsy person and loves camping, "Jeeping (in designated areas, of course!)", winter sports, scuba diving, offshore sailing and photography during his spare time.

BRAZIL

From Page 1

patients.” The meeting reached its climax when the Coalition proudly announced their plan to promote survival of GIST patients, which they called the *Monterrey Declaration*, focused on four key principles:

- To improve the knowledge of patients and physicians.
- To increase patient access to adequate treatment and resources.
- To support local patient support organizations, including the creation of new ones.
- To encourage collaboration and coordination with the physician community.

Since the issue of the *Declaration*, many educational and advocacy efforts

Discussions.”

With much accomplished, there is still much work to do for this dedicated group of patient group leaders. Therefore, this past April, Alianza GIST hosted its second annual meeting in São Paulo, Brazil. Participants included

Sandra Mesri (Argentina), Melisa Biman (Argentina), Vicky Ossio (Bolivia), Diane Waterland (Brazil), Nadir Amaral (Brazil), Piga Fernández (Chile), Rafael Becerra (Colombia), Rafael Vega (Colombia), Michael Josephy (Costa Rica), Alejandro Miranda (Dominican



Local Brazilian GISTers enjoy meeting Alianza GIST reps.

other in the region. Such topics included: GIST treatment and research updates; sharing GIST stories and survival strategies; overview of substandard drugs and advocacy efforts; gaining access to life-saving information, treatment and resources; and country organization updates and strategies for future collaborative work.

For the first part of the meeting, local GIST patients and caregivers were invited to join the group and learn more about their rare disease and speak with others. For most of them, it was the first time meeting another GIST patient

and, needless to say, it was a very emotional event.

At the conclusion of the meeting, Alianza GIST representatives decided to focus on the following areas that needed the most attention:

- Adequate diagnosis
- Access to safe, effective and affordable treatment
- Increased efforts to establish more viable treatment options

Three sub-committees were formed to focus on: 1) Patient-to-Patient Outreach and Support, 2) Patient-to-Doctor Education, and 3) Access to Treatment. Regular teleconferences and webcasts will convene to work on the aims set forth in São Paulo and Monterrey.

With this great roadmap in front of us, the entire Alianza GIST group is enthusiastic to work together and better the lives of GIST patients in Latin America!



Representatives from 12 Latin American countries gathered together in Sao Paulo, Brazil.

have been conducted locally and regionally. Educational materials were produced including the first publication of GIST newsletters and pamphlets in Spanish and Portuguese. New formal organizations were established in countries such as Fundación GISTColombia (www.fundaciongistcolombia.org), Fundación GIST México (www.fundaciongist.org) and Asociación GIST Argentina. Fundación GIST Mexico was able to partner with Tecnológico de Monterrey (the MIT of Latin America) and initiate an online CME accredited GIST training tool in Spanish for Latin American physicians. This program will be officially launched at the upcoming American Society of Clinical Oncology meeting (ASCO) on June 5th where a panel of GIST experts will discuss “Best Practices in Latin America for GIST; Tumor Board: Case

Republic), Rodrigo Salas (Mexico), María Teresa Ponce (Nicaragua), Eva María Ruiz de Castilla (Peru), Ines García-González (The Max Foundation), Norman Scherzer (LRG), Sara Rothschild (LRG), and Tricia McAleer (LRG). Representatives who could not attend were Fabrizio Martilotta (Uruguay) and María Isabel Gómez (Venezuela). Panelists invited to present included Dr. Alexandre Sakano (Universidade de São Paulo Medical School), Dulce Couto (Brazilian National Cancer Institute-INCA), Dr. Marineide Prudencio de Carvalho (Hospital Santa Casa de São Paulo), and Siobhán Ní Bhuachalla (SixDegrees Health Care Consulting).

The meeting covered topics relevant to the Latin American GIST community and provided an opportunity to share best practice experiences and ways to collaborate and coordinate with one an-

GIST, my friend: How to live with this chronic disease day-to-day

By Dr Philippe Fontaine
Swiss GIST Patient

The discovery of a diagnosis of cancer takes us through various different stages, which are the same as those that a patient passes through as he nears death. It starts with denial – “impossible!” – and ends with acceptance. At this stage there is the possibility of rebuilding our lives and changing, while still living with the disease on a day-to-day basis.

Acceptance – for me that means trying to live as positively and naturally as possible by thinking of cancer as a friend and not as an enemy!

How? Simplify your life by obeying your physician’s orders, that is, take your drugs every day by thinking of them as your companions who are going to do you good. The side-effects



will happen. That is tough! Grin and bear these too. A severe cramp is of course painful, but you

know it won’t last long! Edema and a pale complexion, they’re not serious, sun tans are no longer trendy!

It will also be a matter of finding out about your disease and not passively awaiting the information your physician will provide you. Look on the internet but be careful and selective, since the best may border on the worst ... Participate in GIST conferences and do not hesitate to ask questions. The more you know about your disease, the easier

it will be to live with.

But of course we must not forget about living ...indulge yourself! Take that trip you have always dreamed about, treat yourself to small presents, put yourself first!

Get enough sleep, eat healthily, and be more active; these three rules should become high priority. Think about your spirituality, not because it prepares you for death but because it helps you to live!

Finally, try a very simple exercise. Take a sheet of paper, compile two columns, one for the pluses, one for the minuses, then note down what you have lost from this disease and what you have gained by searching honestly deep down inside yourself. And you will probably then discover that one column is immediately fuller than the other!

In this way I hope you will be able to say: I have a new friend: my GIST!

Steve “Da Yooper” Bashaw passes peacefully at 59

Stephen A. Bashaw, age 59 of Ishpeming (Ely Twp) passed away Friday, May 27, 2011 at home under the loving care of his family and UP Home Health & Hospice.

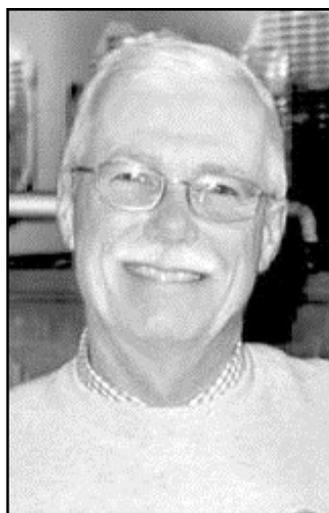
Stephen was born March 12, 1952 in Laurium, MI to Florence (Paquin) and the late George Bashaw. He graduated from Lake Linden-Hubbell High School, class of 1970. Following high school, he served his country in the United States Marine Corp. He was honorably discharged in 1973 after serving in Vietnam. Steve also served in the United States Naval Reserve attached to NMCB-25 out of Fort McCoy, WI having 20 years of service to his country.

Steve worked for Cliffs Natural Resources for 32 years working as a heavy

equipment operator, retiring in 2009. He was a member of St. Joseph Catholic Church. Steve enjoyed fishing, rabbit hunting, tinkering in his garage, and the many adventures he and his wife had riding their Goldwing.

Steve is survived by his wife, and best friend, Laurie (Poissant) Bashaw, whom he married July 27, 1974, his mother Florence Bashaw of Lake Linden, 3 children: Eric Bashaw of

Champion, Stephanie (Matt) Burgess of Arlington, WA and Holly (Tom) Palmer of Marquette. He was a proud Papa to Sebastian & Benjamin Burgess and Sophia Palmer. He is also survived by a sister Judy (Mike)



Drewyvor of Houghton, a brother John (Mary Ann) Bashaw of Plymouth, WI, father and mother-in-law Larry and Joan Poissant of Ishpeming, and several nieces and nephews. Steve was preceded in death by his father George.

Memorial considerations may be directed to the Pan-Mass Challenge for GIST research c/o

Mike Cesarini 2 Settlers Path Duxbury, MA 02332 in memory of Stephen Bashaw.

Steve's obituary may be viewed at www.bjorkandzhulkie.com where his guest book may be signed.



MUTATIONS

From Page 7

much longer progression-free survival time (19 months at 800 mg vs. 6 months at 400 mg) and better response to Gleevec at 800 mg compared to 400 mg. The 2010 NCCN Guidelines says this in reference to metastatic exon 9 dosing of Gleevec, “Patients with documented mutations in KIT exon 9 may benefit from dose escalation up to 800 mg daily (400 mg twice daily) depending upon tolerance”.

Patients with other mutations are given standard dose imatinib (400 mg); however, there is evidence that maintaining Gleevec plasma levels above 1100 ng/mL may significantly increase progression-free survival time for metastatic patients. This hypothesis is best supported for patients with KIT exon 11 mutations, the most common mutation occurring in GIST³.

Adjuvant Treatment

As one factor in deciding on adjuvant Gleevec

Results of the phase III Z9001 adjuvant Gleevec trial have showed significant delays in recurrences when patients are

given 400 mg of Gleevec for one year. However, not all mutation subtypes have shown a benefit. In fact, of the four most common subtypes of GIST only KIT exon 11 mutations have shown a significant benefit (reported at the 2010 conference of the American Society of Clinical Oncologists (ASCO)). PDGFRA D842V mutations are insensitive to Gleevec and Sutent and seem to have a lower recurrence rate that is not reduced by taking adjuvant Gleevec. To date, there has been no significant difference in recurrence for wildtype GIST either. For KIT exon 9 mutations, there appears to be an initial benefit, but the recurrence-free survival curves later crossover showing more late benefit for placebo, raising questions about proper dose and duration of treatment. At best, more

information is needed for KIT exon 9 mutations. We will soon have more information about adjuvant Gleevec as final results of the Scandinavian study comparing one year of adjuvant Gleevec versus three years of adjuvant Gleevec will be presented at the plenary session of the American Society of Clinical Oncologists (ASCO) in June.

Clinical Trials and Mutation-specific Clinics

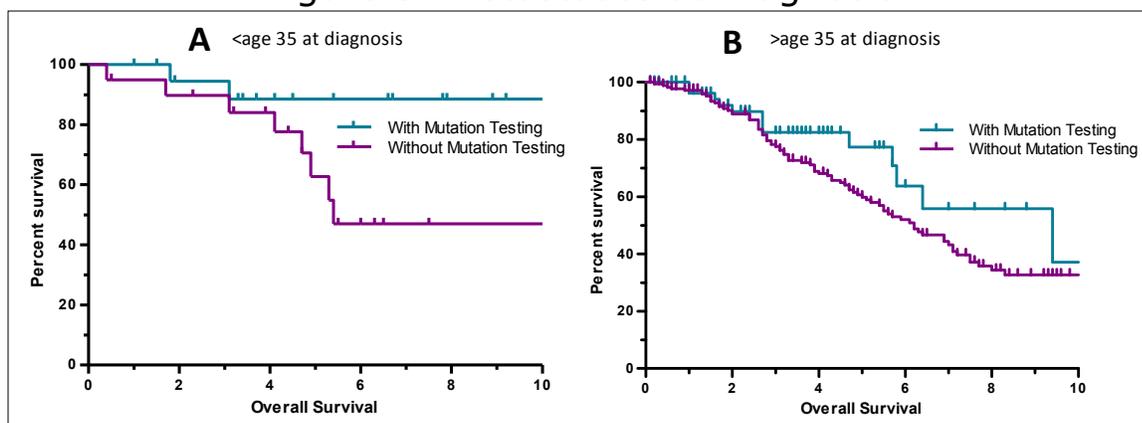
New clinical trials for D842V (open) and wildtype GIST (planned)

A new phase II clinical trial (NCT01243346) for a specific inhibitor of the D842V mutation in PDGFRA is open for recruitment for advanced D842V GIST patients in the United States. The D842V mutation has been the most difficult mutation to target in

GIST appears to be driven by mutations in the SDH complex or inactivation of SDHB, a tumor suppressor gene. Although not a clinical trial, the clinic has also published a poster of pediatric/wildtype response to various kinase inhibitors.

In summary, the United States is falling far behind other countries in terms of mutational testing for GIST patients. This is in spite of guidelines recommending testing, availability of testing through a growing network of labs, and numerous reasons for doing the testing. Mutational testing represents one of the best opportunities to individualize patient treatment. It has the potential to guide dose selection, influence the decision to take or not take adjuvant imatinib, guide patients to specific trials

Figure 5: Metastases at Diagnosis



GIST and makes up about five percent of all GISTs. This is the first trial for a specific mutation in GIST and the first drug therapy option for these patients. Ironically, most patients with this mutation will never be tested and thus never know they are eligible for this trial if current trends in mutational testing continue.

Clinical trials are also being planned for patients with wildtype GIST. Specifically, a trial with a drug that targets the IGF1R receptor is being planned. In addition, patients with wildtype GIST are eligible to attend the Wildtype & Pediatric GIST clinic hosted twice a year by the National Institutes of Health (NIH). This clinic has yielded valuable information about wildtype and pediatric GIST, most notably that pediatric-type

and help refer wildtype and pediatric-type GIST patients to additional resources. In the near future the Life Raft Group will be launching a survey to help us understand why mutational testing is seldom performed in the United States.

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Camaraderie flourishes at New Horizons meeting in Amsterdam



Left: Drs. Paulo Casali of Italy, Jean-Yves Blay of France, Jonathan Fletcher of the United States of America and Peter Reichardt of Germany, chaired a GIST expert panel at the international patient summit, *New Horizons*, held in Amsterdam in May.

Right: The patient reps are attentive at one of the panel discussions at *New Horizons*.
Below: The GIST Steering Committee halts their hard work for a quick photo.



Mark your calendars!

- Are you going to be at ASCO 2011 in Chicago June 2-7? Come visit us at Booth 2010.
- The NIH's Pediatric & Wildtype GIST clinic, held at the National Institutes of Health is already here, **June 15-17**.



Chicago-area GISTers meet!



Chicago-area GIST patients met on May 1, 2011. Pictured from left to right are Bob and Lucy Madsen, Bob and Janet Sholiton, Margi Hughes, Leigh Borland, Carmen and Stan Drab, Thomas Lad, MD, Fred Rosen, MD
Attending but not pictured: Fred Chamanara & Vince Coccia, Dick and Sue Kinzig, Nestor and Beth Sanchez

Science & Surprises abound at NJ GISTers meeting!



Dr. Maki speaks on treatment advances.

On May 7, we held the NJ Chapter Meeting of GISTers at the LRG Office in Wayne, NJ. It was a great gathering of patients, caregivers, LRG staff members and our guest speaker, Dr. Bob Maki of Mt. Sinai Hospital in New York. Dr. Maki gave a nice intro and informational talk about the latest research on the drugs treating GIST and what's new in the fight against this rare cancer. He was very informative and held a Q & A session with us afterward. Everyone participated and shared experiences and concerns and Dr. Maki was wonderful in answering our questions. The

Grand Finale of our meeting was entertainment by Norman Scherzer dressed up in a sailor suit aboard the Life Raft singing "Thank You for Being a Friend" (Check out the video on the LRG Facebook Page)! Dr. Maki jumped in the life raft with Norm and sang along! It was a nice ending to our meeting and left us feeling upbeat and with more hope of finding a Cure to this dreaded disease. Thanks LRG for all you do making sure none of us face this journey alone!

-NJ Chapter Leader, Anita Getler



"Thank you for being a friend, Dr. Maki!"

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